Clean Set of All Pending Claims

(July 17, 2003)

43. (Currently amended) A method for inhibiting VEGF-induced angiogenesis in a subject, comprising administering to said subject an effective amount of a humanized anti-VEGF antibody which (a) binds human VEGF with a K_d value of no more than about 1×10^{-8}M; (b) has an ED50 value of no more than about 5nM for inhibiting VEGF-induced proliferation of endothelial cells *in vitro*; and (c) inhibits VEGF-induced angiogenesis *in vivo*, wherein 5mg/kg of said humanized antibody inhibits at least about 50% of tumor growth in an A673 *in vivo* tumor model.

44. (Currently amended) The method of claim 43, wherein said humanized anti-VEGF antibody binds human VEGF with a K_d value of no more than about 1×10^{-9}M.

45. (Previously presented) The method of claim 43, wherein said subject has a tumor.

46. (Currently amended) The method of claim 45, wherein 5mg/kg of said humanized antibody inhibits at least about 80% of tumor growth in an A673 *in vivo* tumor model.

47. (Currently amended) The method of claim 43, said humanized anti-VEGF antibody having a heavy chain and a light chain, wherein the heavy chain variable domain comprises four framework regions (FR) and three complementarity determining regions (CDR) as a contiguous sequence represented by the formula: FR1-CDRH1-FR2-CDRH2-FR3-CDRH3-FR4, wherein the four FRs are derived from a consensus human antibody heavy chain framework region sequence and the three CDRs are derived from a non-human anti-VEGF antibody, and wherein the light chain variable domain comprises four FRs and three CDRs as a contiguous sequence represented by the formula: FR1-CDRL1-FR2-CDRL2-FR3-CDRL3-FR4, wherein the four FRs are derived from a consensus human antibody light chain framework region sequence and the three CDRs are derived from the non-human anti-VEGF antibody.

49. (Currently amended) The method of claim 47, wherein the heavy chain variable domain comprises the following CDR amino acid sequences: CDRH1 (GYX_IFTX_2YGMN, wherein X_1 is T or D and X_2 is N or H; SEQ ID NO: 128), CDRH2 (WINTYTGEPTYAADFKR; SEQ ID

NO:2) and CDRH3 ($YPX_IYYGX_2SHWYFDV$, wherein X_I is Y or H and X_2 is S or T; SEQ ID NO: 129); and wherein the light chain variable domain comprises the following CDR amino acid sequences: CDRL1 (SASQDISNYLN; SEQ ID NO:4), CDRL2 (FTSSLHS SEQ ID NO:5) and CDRL3 (QQYSTVPWT; SEQ ID NO:6).

50. (Currently amended) The method of claim 47, wherein the heavy chain variable domain comprises the following CDR amino acid sequences: CDRH1 (GYTFTNYGMN; SEQ ID NO:1), CDRH2 (WINTYTGEPTYAADFKR; SEQ ID NO:2) and CDRH3 (YPHYYGSSHWYFDV; SEQ ID NO:3); and wherein the light chain variable domain comprises the following CDR amino acid sequences: CDRL1 (SASQDISNYLN; SEQ ID NO:4), CDRL2 (FTSSLHS SEQ ID NO:5) and CDRL3 (QQYSTVPWT; SEQ ID NO:6).

51. (Currently amended) A method for inhibiting VEGF-induced angiogenesis in a subject, comprising administering to said subject an effective amount of a humanized anti-VEGF antibody which binds human VEGF with a K_d value of no more than about 1×10^{-8}M, said humanized anti-VEGF antibody comprising a heavy chain variable domain sequence of SEQ ID NO:116 and a light chain variable domain sequence of SEQ ID NO:115.

52. (Currently amended) A method for inhibiting VEGF-induced angiogenesis in a subject, comprising administering to said subject an effective amount of a humanized anti-VEGF antibody which binds human VEGF with a K_d value of no more than about 1×10^{-8}M, said humanized anti-VEGF antibody comprising a heavy chain variable domain sequence of SEQ ID NO:7 and a light chain variable domain sequence of SEQ ID NO:8.

53. (Previously presented) The method of claim 43, wherein said humanized anti-VEGF antibody is a full length antibody.

54. (Previously presented) The method of claim 53, wherein said humanized anti-VEGF antibody is a human IgG.

55. (Previously presented) The method of claim 43, wherein said humanized anti-VEGF antibody is an antibody fragment.

56. (Previously presented) The method of claim 55, wherein said humanized anti-VEGF antibody is a Fab.

57. (Previously presented) The method of claim 43, wherein said subject has a retinal disease.

58. (Previously presented) The method of claim 57, wherein said retinal disease is age-related macular degeneration (AMD).

59. (Previously presented) The method of claim 58, wherein the humanized anti-VEGF antibody is administered to the subject at a dose of at least about 0.5mg/kg.

60. (New) The method of claim 47, wherein the heavy chain variable domain FR has at least one substitution wherein the human FR residue is replaced by a corresponding residue from the non-human anti-VEGF antibody, said residue is selected from the following positions: 37H, 49H, 67H, 69H, 71H, 73H, 75H, 76H, 78H and 94H; and wherein the light chain variable domain FR has at least one substitution wherein the human FR residue is replaced by a corresponding residue from the non-human anti-VEGF antibody, said residue is selected from the following positions: 4L, 46L and 71L (positions according to Kabat numbering).